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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/630,235	Applicant(s) RATNER ET AL.	
	Examiner Ann Y. Lam	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *16-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/12/04*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election the species poly(N-isopropylacrylamide) in the response filed June 9, 2006, is acknowledged.

While the last Office action only had a requirement for a species election but did not have any further restriction requirement, the following restriction requirement is found to be appropriate for the reasons set forth below.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-15, drawn to a device for binding cells or molecules, classified in class 436, subclass 518.

II. Claims 16-25 and 31-47, drawn to a method for binding molecules or living cells, classified in class 435, subclass 4.

III. Claims 26-30, drawn to a method for binding more than one type of molecule or more than one type of living cell, classified in class 435, subclass 973.

Inventions I and (II and III) are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used to practice

another and materially different process, such as providing a layer for attachment of probes, or for isolating biomolecules.

Inventions II and III are unrelated and patentably distinct and independent inventions. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are not disclosed as capable of use together and they have different designs, modes of operation and effects because invention II requires that the temperature-responsive material can exist in a first state that binds molecules and can existing in a second state that binds substantially less molecules or living cells than the first state, whereas invention III does not. Invention III requires removing a first type of molecules or living cells that are not bound to a first population of temperature-responsive layers portions, and contacting the temperature-responsive material with a second type of molecules or living cells, whereas invention II does not.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found

allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does

not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Dennis Shelton on June 19, 2006, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 16-47 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is understood that this election is made in addition to the election of the species poly(N-isopropylacrylamide), made in Applicant's response filed June 9, 2006.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Status of Claims

Claims 16-47 are withdrawn.

Claims 1-15 are currently pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-10,12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lahann et al., 7,020,355, in view of Carlson et al., 6,939,515.

As to claim 1, Applicant claims a device for binding cells or molecules, wherein the device comprises: a body defining a first surface and a second surface that is located opposite to the first surface; a heater disposed upon the first surface; and a temperature-responsive layer disposed upon the second surface, wherein the temperature-responsive layer comprises a temperature-responsive material that can exist in a first state that binds molecules or living cells, and can exist in a second state that binds substantially less molecules or living cells than the first state, and wherein the temperature-responsive material is reversibly convertible to the first state from the second state in response to an effective amount of thermal energy.

Lahann et al. disclose the invention substantially as claimed because Lahann et al. teach providing a nanolayer of a material on a substrate and applying an external stimulus to the substrate and that when the stimulus is applied, the nanolayer shifts from a first conformation state, characterized by a first property, to a second conformation state, characterized by a second property (col. 2, lines 38-46). Moreover, Lahann et al. teach that the external stimulus may include application of a change in temperature (col. 2, lines 51-53). Lahann et al. specifically teach reversibly modifying a property of a surface wherein when an external stimulus is applied to the nanolayer and substrate, the nanolayer shifts from a first absorption affinity to a second absorption

affinity (col. 3, lines 44-50). Lahann et al. teach that the surface properties that may be switched using the methods of the disclosed invention include any surface property that a skilled artisan wishes to control (col. 7, lines 11-13),and that the surface properties may also be adjusted to reversibly increase or decrease the affinity of proteins or polynucleotides for the surface (col.7, lines 18-20).

More importantly, it is taught by Lahann et al. that temperature may also be used to modify the conformation of the molecular assembly and that for example an alpha helix of a biomolecule may exhibit a conformation change at a given temperature(col.13, lines 6-9). Lahann et al. teach in column 13, line 59 to column 14, line 1, that the nanolayers of the disclosed invention enable the magnification of a molecular level event. Nanolayers of molecular assemblies designed to switch together in response to a stimulus amplify the chemical effects of the individual assemblies to change a macroscopic surface property (col. 13, lines 60-64). Lahann et al. teach that for example the nanolayers can be constructed to facilitate adhesion of cells and biomolecules in one conformation and to repel the adhered material or to change the organization of deposited biomolecules in a second conformation (col. 13, line 65 – col. 14, line 1).

Lahann et al. further teach that the surfaces of the invention may be used to detect small concentrations of an analyte (col. 24, lines 13-14). A fluid that is being analyzed may be passed over a nanolayer having a carrier to which the analyte will bind or adsorb, and the nanolayer may be used to concentrate the analyte for easier detection or to detect small quantities of the analyte (col. 24, lines 17-19). The analyte may be detected directly or the carrier may have an affinity for an intermediate agent

that has an affinity for the analyte and exhibits a detectable property (e.g., a specific emission or absorption wavelength) when it binds to the analyte (col. 24, lines 19-23). Lahann et al. also teach that by periodically changing the conformation of the nanolayer, the analyte will be released from the detector back into the fluid (col. 24, lines 26-28).

The nanolayer disclosed by Lahann et al. is thus deemed to be the temperature-responsive layer as is claimed by Applicant, wherein the temperature-responsive layer comprises a temperature-responsive material that can exist in a first state that binds molecules or living cells, and can exist in a second state that binds substantially less molecules or living cells than the first state, and wherein the temperature-responsive material is reversibly convertible to the first state from the second state in response to an effective amount of thermal energy. The substrate on which the nanolayer is disposed is deemed to be second surface claimed by Applicant.

However while Lahann et al. teach an external stimulus that causes a change of temperature (col. 2, lines 51-53) which alters the properties of the nanolayer, Lahann et al. do not specifically teach a heater disposed upon a first surface that is located opposite to the surface on which the nanolayer is disposed, as is claimed by Applicant in claim 1.

Carlson et al. however teach an assay device that includes a thermal platform (2810) that can support and controllably heat an array (i.e., a substrate containing samples) (col. 55, lines 6-8, and see fig. 28). Carlson et al. teach that the platform (2810) includes a thermal platform top (2812) and thermal platform base (2814), which when assembled together create a cavity (2816) that supports a substrate or suitable

testing platform (e.g., a carrier plate), (col. 55, lines 11-14). Moreover it is taught by Carlson et al. that the heating elements (2822) may be attached to or embedded in the thermal platform base (2814) to provide a mechanism for heating thermal platform base (2814), (col. 55, lines 64-67). Carlson et al. teach that resistive heating elements (2822) may be embedded or attached to thermal platform base (2814) to permit improved control of thermal control of thermal uniformity or specific temperature profiles in thermal platform (281), (col. 56, lines 3-12). Carlson et al. teach for example that the temperature of the thermal platform containing the substrate and material samples is increased at a defined rate and monitored with one or more temperature sensors in contact with the substrate and that a computer can be interfaced with the heating system to provide feedback for better temperature control (col. 58, lines 7-15).

Thus, Carlson et al. teach a device with a heater disposed on one surface (i.e., 2814) that is located opposite to the surface on which material samples are located (i.e., the substrate or testing platform disclosed in column 55, lines 13-14), (see figure 28). While Lahann et al. teach an external stimulus providing a temperature change but does not disclose the location of the external stimulus with respect to the nanolayer nor any structural details as to this external stimulus, nevertheless it is understood that there is an external stimulus that provides a temperature change. Moreover, Carlson et al. teach a device equipped with a heating element to heat the substrate containing material sample for an assay. Carlson et al. also teach that the device provides the advantage of improved thermal control of thermal uniformity or specific temperature profiles in thermal platform (col. 56, lines 3-12), and that the temperature of the thermal platform

containing the substrate and material samples can be increased at a defined rate and monitored with one or more temperature sensors that is interfaced with a computer to provide feedback for better temperature control (col. 58, lines 7-15). It would have been obvious to one of ordinary skill in the art at the time the invention was made provide a heating element opposite the substrate on which the nanolayer disclosed by Lahann et al.. is disposed, as taught by Carlson et al., as the specific external stimulus generally disclosed by Lahann et al., because Carlson et al. teach that the heating elements in this configuration provides the advantage of improved thermal control of thermal uniformity or specific temperature profiles in thermal platform. Moreover Carlson et al. teach that a further advantage of the heating system includes better temperature control through a temperature monitor and a computer for feedback. Thus it would have been obvious to one of ordinary skill in the art to utilize the heating system in the configuration as taught by Carlson et al. as the specific external stimulus that is only generally disclosed by Lahann et al. particularly in view of the advantages of the heating system as taught by Carlson et al. Thus, given the modifications to the Lahann et al. invention as taught by Carlson et al., the substrate on which the heating elements are disposed is deemed to be the first surface and the substrate on which the nanolayer is disposed is deemed to be second surface, as are claimed by Applicant.

As to claim 2, Applicant claims that the body consists essentially of glass. This is taught by Lahann et al. (col. 7, lines 24-25).

As to claims 3 through 5, Applicant claims the following dimensions. As to claim 3, Applicant claims that the body has a thickness in the range of from 0.0001 mm to

2mm. As to claim 4, Applicant claims that the first surface and the second surface each have an area in the range of from 1 mm square to 5 cm square. As to claim 5, Applicant claims that the device comprises a longest dimension in the range of from 1.0 mm to 5.0 cm. While neither Lahann et al. nor Carlson et al. teach the dimensions of the substrate or heater, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Lahann et al. and Carlson et al. teach the general conditions of the claims because Lahann et al. teach a substrate with a nanolayer of temperature-responsive material and Carlson et al. teach a heating element disposed opposite a substrate containing material samples (such as the Lahann et al. substrate containing the nanolayer with biomolecules). Thus, discovering the workable or optimum range in dimensions of the substrate and heating element involves only routine skill in the art under *In re Aller.*

As to claims 6 and 7, Applicant claims the configurations as follows. As to claim 6, Applicant claims that the first surface and the second surface are both rectangular. As to claim 7, Applicant claims that the first surface and the second surface are both square. It is noted that Lahann et al. disclose an embodiment wherein the substrate is square (see figure 11). Also, while Carlson et al. do not disclose the shape of the substrate on which the heating elements are disposed, it would have been an obvious matter of design choice to form the first surface and second surface in rectangular or square shapes , since such a modification would have involved a mere change in the shape of a component. A change in shape is generally recognized as being within the

level of ordinary skill in the art. *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (The court held that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.)

The following relates to claims 8 and 9. As to claim 8, Applicant claims that the temperature-responsive material is poly(N-isopropylacrylamide), and as to claim 9, Applicant recites that the temperature-responsive material consists essentially of poly(N-isopropylacrylamide). While, Lahann et al. teach in general a nanolayer that is responsive to a change in temperature (col. 2, lines 39-49 and 51-53 and col. 13, lines 6-9), Lahann et al. do not specifically teach what material is being used as the temperature responsive material in the disclosed invention. However the use of poly(N-isopropylacrylamide) is suggested by Lahann et al. for the reasons as follows.

Lahann et al. teach that self-assembled monolayers have been used to control and pattern the properties of a variety of surfaces and Lahann et al. disclose that it has been found that the wetability of a surface may be controlled by changing the temperature around the lower critical solution temperature of poly(N-isopropylacrylamide)-grafts (col. 1, lines 48-58). Lahann et al. teach that however there is very little research concerning controlled switching between different surface properties (col. 1, lines 49-51). Lahann et al. further state that accordingly it is desirable to develop a method by which the surface properties of a self-assembled monolayer structure may be reversibly switched upon application or removal of an external force

field (col. 1, lines 61-64). Then Lahann et al. teach the disclosed invention comprising a nanolayer that shifts from a first conformation state to a second conformation state upon application of an external stimulus (col. 2, lines 38-40), wherein the external stimulus may be a change in temperature (col. 2, lines 51-53), and Lahann et al. teach reversibly modifying the property of the nanolayer by application of the stimulus to shift the nanolayer from a first absorption affinity to a second absorption affinity, such as an affinity for an analyte (col. 3, lines 40-50).

Thus, Lahann et al. teach that controlling properties of a variety of surfaces are known and Lahann et al. specifically give an example of poly(N-isopropylacrylamide as a material in which wetability may be controlled by changing temperature. It is noted that Lahann et al. teach that the wetting behavior is defined by the molecular-level structure of the interface (col. 5, lines 5-8, and see lines 30-33). Lahann et al. then teach use of such materials, more specifically, Lahann et al. teach reversibly modifying the properties of such materials by an external stimulus for assay purposes such as concentrating analyte or detecting small quantities of analyte (see col. 24, lines 17-28). Thus, while Lahann et al. do not specifically teach the use of poly(N-isopropylacrylamide in the disclosed invention, Lahann et al. teach, in general, use of a material that is responsive to temperature (col. 2, lines 51-53), and that a variety of materials that can be controlled are known, including poly(N-isopropylacrylamide, a material in which wetability may be controlled by changing the temperature (col. 1, lines 51-56). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize poly(N-isopropylacrylamide) as the material forming the

nanolayer taught by Lahann et al. to be responsive to temperature change because Lahann et al. teach use of temperature responsive material in general, and Lahann et al. also teach that poly(N-isopropylacrylamide) is a known temperature responsive material. One of ordinary skill in the art would have reasonable expectation of success in utilizing poly(N-isopropylacrylamide) as the temperature responsive material in the invention taught by Lahann et al. because, as disclosed by Lahann et al. (in column 1, lines 51-53), it has been found that the wetability of this material may be controlled. Moreover, Lahann et al. teach that the surface properties that may be switched using the disclosed method include any surface property that a skilled artisan wishes to control, and Lahann et al. give an example of a change in hydrophobicity or hydrophilicity (col. 7, lines 11-14.) Thus, one of ordinary skill in the art would have reasonable expectation of using in the disclosed invention poly(N-isopropylacrylamide), a material that is known to have different wetability properties that can be controlled.

As to claim 10, Applicant claims multiple heaters are disposed upon the first surface. As indicated above regarding the discussion of claim 1, given the modifications to the Lahann et al. invention as taught by Carlson et al., the substrate on which the heating elements are disposed is deemed to be the first surface and the substrate on which the nanolayer is disposed is deemed to be second surface, as are claimed by Applicant. Moreover, Carlson et al. teach multiple heaters (2822), (see fig. 28, and col. 55, line 64).

As to claim 12, Applicant claims that protein molecules are attached to a portion of the temperature-responsive layer located opposite the heater. Proteins molecules

attached to the temperature-responsive layer is disclosed by Lahann et al. (col. 4, lines 43-44, and col. 13, lines 64-66). As indicated above regarding claim 1, the heater is disclosed by Carlson et al.

As to claim 13, Applicant claims the protein molecules are antibody molecules. This is disclosed by Lahann et al. (col. 4, lines 43-44, and 53, and col. 13, lines 64-66).

As to claim 15, Applicant claims that the multiple heaters comprise a first population of heaters and a second population of heaters, and the temperature-responsive layer comprises a first population of portions, located opposite the first population of heaters, and a second population of portions, located opposite the second population of heaters, wherein a first type of protein molecules is attached to the first population of portions, and a second type of protein molecules is attached to the second population of portions.

The substrate on which the heating elements are disposed, as taught by Carlson et al., is deemed to be the first surface and the substrate on which the nanolayer is disposed is deemed to be the second surface, as claimed by Applicant. Moreover, Carlson et al. teach multiple heaters (2822), (see fig. 28, and col. 55, line 64). The first two heaters (2822) disclosed by Carlson et al. in figure 28 are deemed to be part of a first population of heaters, and the next two heaters are deemed to be part of a second population of heaters. As shown by Carlson et al. in figure 28, the heaters are located opposite the testing platform. The temperature-responsive layer that is opposite the first population of heaters is deemed to be the first population of portions, and the temperature-responsive layer that is opposite the second population of heaters is

deemed to be the second population of portions. Moreover, Lahann et al. teach utilizing the nanolayer to facilitate adhesion of biomolecules (col. 13, lines 64-66), and that such biomolecules may be proteins (col. 4, lines 43-44). The protein that is attached to the first population of portions is deemed to be to be a first type of protein, as is claimed by Applicant, and the protein that is attached to the second population of portions is deemed to be a second type of protein.

2. Claims 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lahann et al., 7,020,355, in view of Carlson et al., 6,939,515, and further in view of Manger et al., 5,858,687.

As to claim 11, Applicant claims at least one living cell is attached to a portion of the temperature-responsive layer located opposite the heater. This is taught by Lahann et al. because Lahann et al. teach that the nanolayers can be constructed to facilitate adhesion of cells in one conformation and to repel the adhered material or to change the organization of deposited biomolecules in a second conformation (col. 13, line 64 – col. 14, line 1).

Lahann et al. in view of Carlson et al. disclose the invention substantially as claimed (see above regarding claim 1). Moreover, Lahann et al. teach utilizing the nanolayer to facilitate adhesion of cells (col. 13, lines 64-65), and that the nanolayer can be used for such purposes as concentrating analyte or detecting analyte (col. 24, lines

17-18). However, while Lahann et al. teach use of cells, neither Lahann et al. nor Carlson et al. teach that the cells are live cells.

Manger et al. however teach an assay performed by (a) incubating in the presence of a portion of a sample to be assayed, a culture of cells which express voltage-gated sodium channels, and which are responsive in a dose-dependent manner to sodium-channel-activating toxins with a medium comprising an agent which causes persistent activation of the voltage-gated sodium channel; (b) incubating the culture with a medium comprising an indicator which is acted upon by living cells to generate a discernable result, and (c) observing the culture for an incidence of the result, whereby an observation of the result is correlated with the presence of the toxin in the sample (col. 7, lines 33-44). Moreover, Manger et al. teach that MTT, i.e., (dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide), colorimetric test of cellular metabolism may be incorporated into the assay, to assess cell proliferation and cytotoxicity based upon the metabolism of MTT by mitochondrial dehydrogenase activity in viable cells (col. 11, line 65 – col. 12, line 4). It is taught by Manger et al. that the cells of the invention must be responsive to the selected indicator (col. 7, line 15), and that MTT is metabolized only in living cells, whose mitochondria cleave its tetrazolium ring to produce a blue-colored formazan product (col. 7, lines 27-29).

Thus, Manger et al. teach an assay using live cells for purposes such as determining the presence of a toxin, or to assess cell proliferation and cytoxicity. It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the assay device taught by Lahann et al. in view of Carlson et al. using

not just cells in general, as is taught by Lahann et al. (col. 13, lines 64-65), but specifically live cells, as taught by Manger et al. because Manger et al. teach that assay of live cells provide the benefit of determining the presence of a toxin, or of assessing cell proliferation and cytotoxicity. That is, one of ordinary skill in the art would recognize the benefit of determining the presence of a toxin, or of assessing cell proliferation and cytotoxicity, for medical or clinical purposes. Moreover, one of ordinary skill in the art would have reasonable expectation of success in utilizing live cells in the Lahann et al. invention because Lahann et al. teach in general that cells can be used with the invention.

As to claim 14, Applicant claims that the multiple heaters comprise a first population of heaters and a second population of heaters, and the temperature-responsive layer comprises a first population of portions, located opposite the first population of heaters, and a second population of portions, located opposite the second population of heaters, wherein a first type of living cell is attached to the first population of portions, and a second type of living cell is attached to the second population of portions. And as previously discussed above regarding claim 11, the cells being live cells are taught by Manger et al. Also, as indicated above regarding the discussion of claim 1 and claim 10, given the modifications to the Lahann et al. invention as taught by Carlson et al., the substrate on which the heating elements are disposed is deemed to be the first surface and the substrate on which the nanolayer is disposed is deemed to be second surface. Moreover, Carlson et al. teach multiple heaters (2822), (see fig. 28, and col. 55, line 64). The first two heaters (2822) disclosed by Carlson et al. in figure 28

are deemed to be part of a first population of heaters, and the next two heaters are deemed to be part of a second population of heaters. As shown by Carlson et al. in figure 28, the heaters are located opposite the testing platform. The temperature-responsive layer that is opposite the first population of heaters is deemed to be the first population of portions, and the temperature-responsive layer that is opposite the second population of heaters is deemed to be the second population of portions. Moreover, Lahann et al. teach utilizing the nanolayer to facilitate adhesion of cells (col. 13, lines 64-65). The cell that is attached to the first population of portions is deemed to be to be a first type of cell, and the cell that is attached to the second population of portions is deemed to be a second type of cell.

Lahann et al. do not teach however that the cells of the first population is a first type of cell and the cells of the second population is a second type of cells. However Lahann et al. do teach an embodiment of the disclosed invention wherein different molecular assemblies having different compositions may be incorporated into a single nanolayer, and the assemblies may be disposed substantially randomly within the nanolayer or alternatively the molecular assemblies may be deposited in separate regions by composition, and the external stimulus may be separately applied to the individual regions (col. 3, lines 8-14). Thus Lahann et al. suggest that the nanolayer may have different molecular assemblies that are different in different regions and stimulated separately in the individual regions. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide different cells in different regions because Lahann et al. suggest that different molecular assemblies may

be provided in separate regions and stimulated separately. That is, one of ordinary skill in the art would recognize that the teaching of different molecular assemblies in separate regions taught by Lahann et al. may be applied to other embodiments such as one using cells, as would be desirable for versatility or convenience.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Ann Lam